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EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,920	VAN BOMMEL ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/3/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6 and 15-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6 and 15-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement of Receipt

Applicant's Response, filed 11/3/2009, in reply to the Office Action mailed 8/5/2009, is acknowledged and has been entered. Claims 1-5 and 7-14 have been cancelled. Claims 6, 15 and 16 have been amended. Claims 17-33 are newly added. Claims 6 and 15-33 are pending and are examined herein on the merits for patentability.

Response to Arguments

Any rejection not reiterated herein has been withdrawn as being overcome by amendment.

Applicant's arguments have been fully considered but they are not persuasive, for reasons set forth hereinbelow.

Double Patenting

Claims 6 and 15-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of copending Application No. 11/719,310. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to contrast agents comprising metal nanoparticles having acoustic impedance above 35.1^5 g/cm^2s and ultrasonic imaging methods therewith. The particles of the '310 Application are encapsulated in a non-proteinaceous biocompatible or biodegradable matrix particle

and/or attached to a non-proteinaceous biocompatible or biodegradable matrix particle, the matrix of the matrix particles being selected from the group consisting of a carbohydrate, a lipid, a synthetic polymer, an aqueous liquid, a surfactant and an organic liquid, or a mixture thereof. Claims 23 and 24 of the instant Application require a coating, which may be selected from natural or synthetic carbohydrates, synthetic polyaminoacids, or physiologically tolerable synthetic polymers or derivatives thereof. Accordingly, the claims are overlapping in scope and are obvious variants of one another. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's response that previously cited Application Serial No. 11/917,310 is drawn to a method and system for assisting flight control of a low-flying aircraft and request for withdrawal of the non-statutory obviousness-type double patenting rejection is acknowledged. It is noted that citation to 11/917,310 was an inadvertent typographical error, and Applicant's copending Application Serial No. 11/719,310 is hereby addressed.

New Grounds for Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Babu *et al.* (*J. Mat. Sci. Lett.*, 2003, 22, p. 1755-1757).

Babu discloses preparation of rhenium nanoparticle dispersions (page 1755). It is noted that the recitation of the intended use of rhenium nanoparticles as a contrast agent has not been given patentable weight to distinguish over Babu because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Since Babu discloses compounds that are the same as those claimed, they would be capable of performing the intended use, as claimed.

It is noted that the functional recitation that the nanoparticles have "an acoustic impedance above 35.10^5 g/cm^{2}s" is not given patentable weight to distinguish over Babu. "Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The

"discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." See *Atlas Power Co. v. Ireco Inc.*, 51 USPQ 2d 1943, 1947 (Fed. Cir. 1999). Therefore, merely claiming a new use, new function, or new property, which is inherently present in the prior art does not make the claim patentable. See *In re Best,* 195 USPQ 430, 433 (CCPA 1977), and MPEP § 2112.

Claim 6 is rejected under 35 U.S.C. 102(e) as being anticipated by Hainfeld *et al.* (US 2005/0020869).

Hainfeld discloses metal nanoparticles of 0.5 to 400 nm (abstract). Metals which can be used to form the metal nanoparticles include rhenium (paragraph 0019). It is noted that the functional recitation that the nanoparticles have "an acoustic impedance above 35.10^5 g/cm^2s" is not given patentable weight to distinguish over Hainfeld. "Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The "discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." See *Atlas Power Co. v. Ireco Inc.*, 51 USPQ 2d 1943, 1947 (Fed. Cir. 1999). Therefore, merely claiming a new use, new function, or

new property, which is inherently present in the prior art does not make the claim patentable. See *In re Best,* 195 USPQ 430, 433 (CCPA 1977), and MPEP § 2112.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15-29, 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hainfeld *et al.* (6,818,199), in view of .West *et al.* (US 2002/0103517).

Hainfeld discloses metal nanoparticles that are useful for enhancing the contrast of x-rays or other radiation sources (abstract). In a preferred form is a medical imaging method and contrast agent which contrasts a targeted portion of a body of a living animal. The method includes intravenously administering a quantity of nanoparticles sufficient to contrast the targeted portion of the body under irradiation and irradiating the targeted portion of the body with penetrating radiation. Each of the nanoparticles has a metallic core surrounded by a surface layer including a component having an affinity for the targeted portion of the body (column 4, lines 53+). The metal nanoparticles have a core composed of gold, platinum, palladium, thallium, bismuth, osmium, iridium, silver, tungsten, lead, tantalum, or uranium. The component of the material of the surface layer may be for example, an antibody, an antibody fragment, a

peptide, a lipid, a carbohydrate, a nucleic acid, or a drug (column 5, lines 1-10). One such preferred gold compound synthesized and found to be useful is a gold nanoparticle with a gold core approximately 2 nm in diameter, which contains about 240 gold atoms. "Metal particle" or "metal nanoparticle" are defined to be all constructs having a metal core ranging from 0.5 to 500 nm in size. "Gold particle" or "gold nanoparticle" are defined to be all constructs having a gold core ranging from 0.5 to 500 nm in size. Larger or smaller gold compounds, clusters, particles and colloids may also be utilized, e.g. gold colloids that are typically characterized by their gold diameter (from 0.5 nm to 100 nm) (column 6, lines 8-20). The outer surface shell of material may include a directing moiety or more than one directing moiety for specific targeting, such as an antibody, antibody fragment, peptide, lipid, carbohydrate, nucleic acid, drug, or other molecule. In addition, it is possible to couple further components to the shell material. By such means, the directing moieties such as antibodies or peptides may be attached. They may be directly coupled to the core by attachment through a sulfur atom, for example; alternatively they may be covalently coupled to the organic shell; additionally, they may be adsorbed non-covalently to the particle or particle shell (column 9, lines 50+). In addition to x-rays, other forms of electromagnetic probes may be employed to detect or image the agents. This includes, but is not limited to, the use of: static magnetic fields, visible light, lasers, ultrasound (column 19, lines 10-15).

It is noted that the limitation of the instant claims wherein the particle has "an acoustic impedance above 35.1^5 g/cm^2s" is not given patentable weight to distinguish over Hainfeld. "Products of identical chemical composition cannot have mutually

exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The "discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." See *Atlas Power Co. v. Ireco Inc.*, 51 USPQ 2d 1943, 1947 (Fed. Cir. 1999). Therefore, merely claiming a new use, new function, or new property, which is inherently present in the prior art does not make the claim patentable. See *In re Best,* 195 USPQ 430, 433 (CCPA 1977), and MPEP § 2112. In the instant case, since Hainfeld teaches materials which have the same structural features as those claims, it is interpreted absent evidence to the contrary, that they would also have the claimed functional properties of acoustic impedance. This interpretation is supported by Applicant's specification, which teaches that acoustic impedance (Z) is defined as the product of density (ρ) and speed of sound (c) in a medium (paragraph 0028), and that examples of metals with an acoustical impedance which is appropriate in the context of the present invention are gold, silver, platinum, palladium, tungsten or tantalum, rhenium, or a mixture thereof (paragraph 0029).

Hainfeld does not specifically recite in vitro imaging. It is for this reason that West is joined.

West discloses localized delivery of heat and the localized imaging of biological materials. The delivery may be in vitro or in vivo and is useful for the localized

treatment of cancer, inflammation or other disorders involving overproliferation of tissue. The method is also useful for diagnostic imaging (abstract). Nanoparticles include gold-containing nanoparticles (see claim 5). Methods of diagnostic imaging of cell or tissue comprising the steps of delivering nanoparticles to the cell or tissue and exposing said nanoparticles to radiation selected from the group consisting of ultrasound, magnetic fields, and electric fields are disclosed (see claim 33). With respect to instant claim 29, West discloses oral administration, including capsules.

It would have been obvious to one of ordinary skill in the art at the time of the invention to employ the particles of Hainfeld for methods of in vivo or in vitro imaging when the teaching of Hainfeld is taken in view of West. Both Hainfeld and West are directed to gold-containing nanoparticles and methods of imaging/therapy, including ultrasound. West teaches that structurally similar particles are useful for in vivo and in vitro imaging, and one would have been motivated to use the particles of Hainfeld for in vitro imaging of cells and tissues in order to expand the applications for which the particles are useful. With respect to the limitation that diagnosis or imaging are achieved by applying an ultrasonic wave and receiving ultrasonic sound waves, such steps would be inherent and necessary in the process of ultrasonic imaging disclosed in Hainfeld and/or West.

With respect to the Hainfeld reference, Applicant argues on pages 6-7 of the Response that Hainfeld explicitly discusses forms of electromagnetic radiation, and that there appears to be no disclosure or suggestion in Hainfeld of acoustic properties of the discussed nanoparticles or using such acoustic properties in imaging. Applicant asserts

that Hainfeld is totally focused on the electromagnetic properties for x-ray imaging, and that one can only conclude that Hainfeld is referring to subsonic electromagnetic waves. No argument was set forth with respect to the West reference.

This is not found to be persuasive. It is acknowledged that ultrasonic sonic waves are not formally classified as being an electromagnetic probe. However, Hainfeld specifically recites ultrasound in conjunction with "x-rays, other forms of electromagnetic probes may be employed to *detect or image the agents*," which includes ultrasound. Applicant's assertion that Hainfeld is referring to subsonic electromagnetic waves is not found to be persuasive because Hainfeld specifically recites ultrasound (which is distinct from subsonic waves), and also because ultrasound is disclosed in the context of imaging/diagnostics. Ultrasound is very well known in the in vivo diagnostic arts via use of contrast agents, while subsonic waves are not. This interpretation is further supported by Hainfeld's patent US 5,360,895, drawn to gold clusters (nanoscale) which states that gold can be detected in ultrasonic imaging (column 4, line 43).

Claims 15-23, 25-28, 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bekeredjian *et al.* (*Ultrasond in Med. and Biol.*, 2002, 28(5), p. 691-695).

Bekeredjian discloses gold-bound microtubules as ultrasound contrast agent. Gold colloid was immobilized on protein microtubule walls. Gold-bound microtubules provide a persistent contrast effect, suggesting their use as an ultrasonic contrast agent

with the feasibility of antibody conjugation (abstract). Gold particles were 10 nm (page 692). With respect to instant claim 25, targeted drug delivery is also disclosed (page 695).

It would have been obvious to one of ordinary skill in the art at the time of the invention to extend the teachings of Bekeredjian to in vivo/in vitro ultrasonic imaging, since Bekeredjian specifically teaches that his compositions are intended for use as ultrasound contrast agents, and one would have had a reasonable expectation of success in doing so since Bekeredjian teaches that his compositions provide advantages such as a persistent contrast effect. With respect to the limitation that diagnosis or imaging are achieved by applying an ultrasonic wave and receiving ultrasonic sound waves, such steps would be inherent and necessary in the process of ultrasonic imaging (see page 692).

Applicant argues on page 7 of the Response that Bekeredjian does not disclose the same particles as in the present application and in particular claim 15. Applicant asserts that the present specification discloses solid metal particles that are not associated with non-metallic compounds such as proteins, polysaccharides and other structuring compounds, and that these characteristics permit the particles to have an acoustic impedence above 35.10^5 g/cm^{2}s. Applicant contends that Bekeredjian's particles do not have theses properties, instead disclosing gold-bound microtubules.

This is not found to be persuasive. Dependent claims 23 and 24 of the instant claims include nanoparticles associated with coating such as polyaminoacids, etc. Therefore the mere presence of additional components does not appear to preclude

nanoparticles from having the claimed acoustic impedence. In addition, Applicant's specification, discloses that acoustic impedance (Z) is defined as the product of density (p) and speed of sound (c) in a medium (paragraph 0028), and that examples of metals with an acoustical impedance which is appropriate in the context of the present invention are gold, silver, platinum, palladium, tungsten or tantalum, rhenium, or a mixture thereof (paragraph 0029). 10 nm gold nanoparticles in the compositions of Bekeredjian inherently have the requisite density, therefore absent evidence to the contrary, the particles would also have the claimed acoustic impedence.

See also MPEP 2145. If a *prima facie* case of obviousness is established, the burden shifts to the applicant to come forward with arguments and/or evidence to rebut the *prima facie* case. See, e.g., In re *Dillon,* 919 F.2d 688, 692, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990). Rebuttal evidence and arguments can be presented in the specification, *In re Soni*, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995), by counsel, *In re Chu*, 66 F.3d 292, 299, 36 USPQ2d 1089, 1094-95 (Fed. Cir. 1995), or by way of an affidavit or declaration under 37 CFR 1.132, e.g., *Soni*, 54 F.3d at 750, 34 USPQ2d at 1687; *In re Piasecki*, 745 F.2d 1468, 1474, 223 USPQ 785, 789-90 (Fed. Cir. 1984). However, arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., *In re Huang*, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984).

Claims 6 and 15-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hainfeld *et al.* (6,818,199), in view of West *et al.* (US 2002/0103517), further in view of Hainfeld *et al.* (US 2005/0020869).

The rejection over Hainfeld '199 in view of West is applied as above. It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute rhenium for gold, silver, etc. metal nanoparticles used in Hainfeld and/or West, when the teachings are taken in view of Hainfeld (US 2005/0020869).

Hainfeld (US 2005/0020869) teaches metal nanoparticles of 0.5 to 400 nm (abstract). Metals which can be used to form the metal nanoparticles include rhenium (paragraph 0019). For example, metals which can be used to form nanoparticles suitable for enhancing radiation effects are heavy metals, or metal with a high Z number, including but not limited to gold, silver, platinum, palladium, cobalt, iron, copper, tin, tantalum, vanadium, molybdenum, tungsten, osmium, iridium, rhenium, hafnium, thallium, etc. (paragraph 0019-20). Forms of energy suitable for interaction with the particles includes ultrasound (paragraph 0116).

Accordingly, Hainfeld '199, West and Hainfeld (US 2005/0020869) are drawn to high z metal nanoparticles. The use of such particles for use in diagnostic imaging, including x-ray, ultrasound, etc is disclosed in Hainfeld '199 and West. One of ordinary skill could have substituted one known high z metal nanoparticle (e.g. rhenium for gold, silver, etc.) for use in imaging methods of Hainfeld and/or West, including ultrasonic imaging, and the result would have been predictable, since Hainfeld (US

2005.0020869) teaches rhenium to be functionally equivalent to gold and other metal nanoparticles, including for interaction with forms of energy including ultrasound.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is (571)272-9928. The examiner can normally be reached on Monday-Tuesday and Thursday-Friday 9 AM-5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS